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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/466,921	06/06/95	ALIZON M	03459.0008-0

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EXAMINER	
PARKIN, J	
ART UNIT	**PAPER NUMBER**
1813	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

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Office Action Summary	Application No. 08/466,921	Applicant(s) Alizon et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Group Art Unit 1813

☒ Responsive to communication(s) filed on *5/30/97* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *28, 29, and 32-45* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28, 29, and 32-45* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Amendment

37 C.F.R. § 1.129(a)

1. Since this application is eligible for the transitional procedure of 37 C.F.R. § 1.129(a), and the fee set forth in 37 C.F.R. § 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 C.F.R. § 1.129(a). Applicant's submission after final filed on May 30, 1997, has been entered. Claims 23-27, 30, and 31 were canceled without prejudice or disclaimer, claim 28 amended, and new claims 32-45 submitted. Claims 28, 29, and 32-45 are pending in the application.

35 U.S.C. § 112, First Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 39-45 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is apparent that the λ-J19 LAV molecular clone is required to practice the claimed invention. Since the molecular clone is a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or

available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the λ-J19 LAV molecular clone pursuant to 37 C.F.R. §§ 1.801-1.809. The specification does not provide a repeatable method for obtaining proviral molecular clones with the precise restriction fragments disclosed in Figure 2. Moreover, the lentiviruses are known to exist as a quasispecies, and display considerable genetic heterogeneity, even within the same patient (Goodenow *et al.*, 1989; Holland *et al.*, 1992; and Gao *et al.*, 1994). Accordingly it seems extremely improbable that the skilled artisan would be able to isolate and prepare molecular clones containing the same genotype as the clone disclosed in Figure 7.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If the deposits have not been made under the provisions of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

> (a) during the pendency of the application, access to the deposits will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(c) the deposits will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification. See 37 C.F.R. §§ 1.803-1.809 for additional explanation of these requirements. See also *In re Lundak*, 773 F.2d 1216, 227 U.S.P.Q. 90 (Fed. Cir. 1985).

4. Claims 28, 29, and 32-38 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Newly submitted claims 32-38 are directed toward HIV-1 DNA restriction fragments. The disclosure provides preliminary restriction maps of LAV cDNA (e.g., pLAV75, pLAV82 and pLAV13) and lambda phage clones (e.g., λJ19 and λJ81) (refer to Figures 1 and 2). The restriction coordinates are disclosed on page 4, as well as a series of restriction fragments believed to correspond to the *gag*, *pol* and *env* coding regions (e.g., *Pst*I (800 nt)/*Kpn*I (3500 nt); *Kpn*I(3,500 nt)/*Bgl*II (6,500 nt); *Kpn*I (6,100)/*Bgl*II (9150)). The specification does not disclose, *ipsis verbis*, HIV/LAV viral clones or restriction fragments obtained from

any other viral isolate.

The claimed invention encompasses any HIV-1 DNA restriction fragment having the indicated restriction sites. However, the disclosure fails to provide any guidance pertaining to the identification and characterization of restriction fragments obtained from disparate HIV-1 isolates or strains. It is art-recognized that the *Lentivirinae* display considerable genomic heterogeneity and exist as a quasispecies (Goodenow *et al.*, 1989; Holland *et al.*, 1992; and Gao *et al.*, 1994). Holland and colleagues concluded (refer to Summary, page 16) that "**RNA virus mutation frequencies generally approach maximum tolerable levels, and create complex indeterminate quasispecies populations in infected hosts.** This usually favors extreme rates of evolution, although periods of relative stasis or equilibrium, punctuated by rapid change may also occur (as for other life forms). **Because complex quasispecies populations of RNA viruses arise probalistically and differentially in every host, their compositions and exact roles in disease pathogenesis are indeterminate** and their directions of evolution, and the nature and timing of "new" virus outbreaks are unpredictable." [Emphasis added by Examiner].

Goodenow and colleagues examined HIV genetic diversity using a novel amplification assay. The authors reported (refer to DISCUSSION, pages 349-351) that:

> RNA viruses have been described as quasispecies (1, 20, 21), i.e., there is no such thing as a viral sequence per se but sets of clusters of closely related sequences. Such is the case for HIV. From any set of data that has been derived, **it was simple to calculate that every HIV viral genome within an isolate was unique. This in turn meant that the rate of nucleotide minsincorporation was greater than 1 X 10^{-4}/base/cycle of replication . . . The potential of the HIV-1**

> **virus to change is thus enormous . . . In conclusion, we are faced by a virus of enormous complexity, certainly more heterogeneous than influenza A or poliovirus (24).** The data described here suggest that there may be as many viral strains of HIV-1 as there are carriers . . . **The possibility of viral mixtures within isolates as well as the high frequency of apparently defective genomes render the task of the molecular biologist difficult.** The impact of such diversity upon the immune system has to be defined. Only by concentrating on active site residues might it be possible to develop general strategies for controlling HIV infection.

Finally, Gao and associates utilized PCR methodologies to examine the genomic heterogeneity of HIV-2 isolates and reported (refer to Abstract, page 7433) that "**These results indicate that the genetic and biologic diversity of HIV-2 is far greater than previously appreciated and suggest that there may be subtype-specific differences in virus biology.**"

Thus, the skilled artisan could reasonably conclude that each HIV-1 viral isolate will display a unique genotype. It is not readily manifest that other HIV-1 isolates, in addition to the LAV isolate disclosed in the specification, will contain the same restriction sites. In view of the prior art, one would expect each isolate to contain a unique restriction map. Absent further guidance from the specificaiton, it would require undue experimentation to practice the invention as presently claimed. *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986).

35 U.S.C. § 112, Second Paragraph

5. Claims 28, 29, and 32-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

These claims contain the recitation "at approximately" in reference to the location of particular HIV-1 restriction sites. This recitation precludes identification of the precise location of said restriction sites. For example, would a *Bam*HI site at 8,000 nucleotides be encompassed by the claim language? Would a site at 8,100 nucleotides be included? Accordingly, the metes and bounds of the patent protection desired can not be ascertained. Applicants may obviate this rejection by reciting the source of the restriction fragment (i.e., clone λJ19) and precise location of the restriction site (i.e., at nucleotide 8150).

Correspondence

6. Correspondence related to this application may be submitted to Group 1813 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Group 1813 is **(703) 305-7939. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.**

7. Any inquiry concerning this communication should be directed to **Jeffrey S. Parkin, Ph.D.**, whose telephone number is **(703) 308-2227**. The examiner can normally be reached Monday through Friday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, **Donald E. Adams, Ph.D.**, can be reached at **(703) 308-0570**. Any inquiry of a general nature or relating to the

status of this application should be directed to the Group 1813 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1813

June 20, 1997

DONALD E. ADAMS
PRIMARY EXAMINER
GROUP 1800